



In the Specification

Please amend the specification at page 1, line 10 as follows:

~~now issued US Patent No. 5,843,462~~

Please amend the paragraph beginning on line 2 of page 12 as follows:

Figure Figures 1A-B. Nasal administration of synthetic TACChR epitopes $\text{T}\alpha\delta 50-169$, $\text{T}\alpha\delta 81-200$ and $\text{T}\alpha\beta 360-378$ causes T cell unresponsiveness to those epitopes. Mice were given two nasal administrations of peptide $\text{T}\alpha\delta 50-169$ (panel Figure 1A, dotted white columns), or α pool (panel Figure 1B, white columns), or peptide-free PBS (black hatched columns) prior to immunization with the peptide(s) used for the nasal treatment. Seven-ten days after the last immunization, the proliferative response of spleen T cells to the immunizing peptide(s) and to TACChR was tested. The data depicted are the results obtained for one mouse from each group, which is representative of the results obtained for all mice of that group. The response induced by 10 μg of PHA is also shown. The columns represent the average S.I. of triplicate cultures. The average c.p.m. obtained in the absence of any stimulation were 297 ± 59 in experiment A and $2,884 \pm 106$ in experiment B.

Please amend the paragraph beginning on line 14 of page 12 as follows:

Figure Figures 2A-B. Nasal administration of synthetic TACChR CD4+ epitope peptides inhibits EMG. Peptide $\text{T}\alpha\delta 50-169$, α pool or peptide-free PBS was administered nasally twice prior to immunization with TACChR, and at different time intervals during the course of the immunization (monthly, panel Figure 2A; weekly, panel Figure 2B). Three immunizations with 50 μg of TACChR, one month apart, were also administered. The data depict the muscle strength of the mice after the third TACChR injection. Muscle strength is measured as holding time using the curare sensitized hanging test described hereinbelow (see Example I). "Normal" mice were mice having a holding time of eight minutes or more; moderately sick mice were those with holding times between four and eight minutes; and severely sick mice were those with holding times of less than four minutes. The four and eight minute levels are indicated by dashed horizontal lines. The panel marked "naive" depicts the values obtained for the mice prior to

immunization with TAChR. The other plots depict the results obtained for mice sham-tolerized with PBS or mice tolerized with peptide α 150-169 or with α pool, as indicated above the plots. The average holding time \pm S.D. of the different groups is indicated, as is the level of significance of the difference compared to the sham-tolerized group (** P<0.002; * P<0.02).

Please amend the paragraph beginning on line 3 of page 13 as follows:

Figure Figures 3A-D. Spleen T cells from mice treated nasally with synthetic TAChR T epitope sequences and immunized with TAChR respond minimally to peptide α 150-169 and respond to the TAChR to a lesser extent than the T cells from sham-tolerized controls. Mice received weekly nasal administrations of peptide-free PBS (circles), α 150-169 (squares) or α pool (triangles) as indicated below of each plots, and were immunized three times with TAChR. The spleen T cells of individual mice were tested in proliferation assays with TAChR (Figure 3A) or individual peptides, i.e., α 150-169 (Figure 3B), α 181-200 (Figure 3C) or α 360-378 (Figure 3D). The data are the average S.I. \pm S.D. of triplicate cultures. The c.p.m. in the absence of any stimulation were 190 ± 88 . The proliferative responses of mice that had EMG are indicated with black symbols. The average responses of the different groups, and the level of significance of the difference between peptide-tolerized and sham-tolerized mice, are shown (**P<0.01; *P<0.03).

Please amend the paragraph beginning on line 16 of page 13 as follows:

Figure Figures 4A-C. Mice treated nasally with TAChR peptides have less serum anti-TAChR antibodies than sham-tolerized mice. The concentration of anti-TAChR antibodies in the sera of individual mice was determined at 4 (Figure 4A), 8 (Figure 4B) and 10 (Figure 4C) weeks after the first TAChR immunization. Mice were tolerized by weekly inhalations (protocol B) of peptide α 150-169 (squares), α peptide pool (triangles) or sham-tolerized with peptide-free PBS (circles), and immunized three times with TAChR, as indicated above the plots. The antibody concentration is expressed as μ M precipitated 125 I- α -bungarotoxin (BTX) binding sites. Mice that presented EMG symptoms are indicated by black symbols. The average antibody concentrations of the different groups and the level of significance of the difference between peptide-tolerized and sham-tolerized mice are indicated.

Please amend the paragraph beginning on line 27 of page 13 as follows:

Figure Figures 5A-B. Nasal administration of synthetic DTX peptides does not affect the development of EMG or the anti-AChR T cell response. Figure 5A) Muscle strength of individual mice. Mice were treated nasally with α pool or DTX peptides and their muscle strength measured after the third TAChR injection as described in the legend to Figure 2. The 4- and 8- minute levels are indicated by dashed horizontal lines. Figure 5B) Proliferative response to TAChR (5 and 10 μ g, as indicated) of triplicate cultures of pooled spleen T cells of four mice from each group, after the third TAChR immunization (white columns, α -pool treated mice; ~~black~~ hatched columns, DTX peptide treated mice). The columns represent average S.I. \pm S.D. of triplicate cultures. The c.p.m. in the absence of any stimulation were 228 ± 29 for the DTX peptide-tolerized mice, and 190 ± 17 for the α -pool tolerized mice.

Please amend the paragraph beginning on line 9 of page 14 as follows:

Figure Figures 6A-B. The reduction of the *in vitro* response to TAChR of spleen T cells from AChR peptide-tolerized mice is reversed by IL-2 treatment. After the third TAChR injection, spleen T cells of mice sham-tolerized (Figure 6A) or tolerized (Figure 6B) with the α pool were pooled, incubated with (~~black~~ hatched columns) or without (white columns) IL-2, and tested in a proliferation assay for their response to TAChR. The columns represent average S.I. \pm S.D. of sextuplicate cultures. The c.p.m. in the absence of any stimulation were 410 ± 124 for the sham-tolerized mice, and 366 ± 78 for the (α pool-tolerized mice). The star indicates a significant difference of the proliferative response of cells treated with IL-2, as compared with the non treated cells ($P<0.0001$).

Please amend the paragraph beginning on line 19 of page 14 as follows:

Figure Figures 7A-B. Nasal treatment with AChR peptides stimulates AChR specific Th2 cells. Secretion of IL-2 (Figure 7A) and IL-10 (Figure 7B) in response to challenge with TAChR (10 μ g) by pooled spleen T cells of 4 mice treated nasally (protocol B) with PBS (white columns) or a pool (~~black~~ hatched columns), after three TAChR injections. Controls were cultures that did not receive any stimulus. The columns represent the average ($n=6$) of the data

obtained 24 hours after TACChR addition to the culture for IL-2, 48 hours for IL-10. The data are expressed as O.D. units detected in ELISA.